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RELATION OF THE *BACILLUS MUCOSUS CAPSULATUS* GROUP TO RHINOSCLEROMA, AND OF THE VARIOUS MEMBERS OF THE GROUP TO ONE ANOTHER.*

ROGER G. PERKINS.

(From the Pathological Laboratory of Western Reserve Medical School, Cleveland, Ohio.)

DURING a former study of the so-called *B. mucosus capsulatus*, published in this *Journal* in 1904, questions concerning the relation of the variety known as the rhinoscleroma bacillus to the disease of that name, came prominently into view. Absence of material other than cultures from outside sources made further investigations impracticable, until the appearance of an undoubted case in Cleveland in 1905.

The literature on the group of organisms and on the disease of rhinoscleroma is very extensive, and has been too often reviewed to make a discussion necessary here. The most comprehensive summary is that of Hasslauer,[1] and a study of his article and of others shows certain points of universal agreement and some points concerning which various authors markedly disagree.

The disease itself is a proliferative lesion of the upper respiratory tract, often extending as low as the larynx. It is confined to man, occurs endemically in eastern Austria and adjacent countries, sporadically in Europe and Asia, and even less frequently elsewhere. The vast majority of cases occur among Slavs. It is apparently non-contagious, or very slightly contagious, for sporadic cases in new places are apparently imported and do not set up foci of infection. Further, with one or two doubtful exceptions, experiments in transmission to animals have been uniformly unsuccessful.

The lesions are in the form of soft, grayish masses which may reach large size, and on histological examination are found to be of the infectious granuloma type, made up of new-formed vascular granulation tissue with a varying amount of old and new fibrous tissue. Near the surface, and, to a less extent, deeper in the lesion,

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[1] *Centralbl. f. Bakt.*, 1904, 37, p. 1.

are hyaline areas, many of which contain masses of bacilli, singly or in pairs, often with well-marked capsules. These areas are said by most writers to be cells which have undergone degeneration, while some consider them to be lymph spaces. These areas are usually known as Mikulicz cells, and held to be histological characteristics of the disease.

The presence of organisms in the tissues led to extensive cultural experiments, with the result that in all cases of the disease bacilli of the mucosus capsulatus group were found. Before bacteriological differentiations reached their present detail, no discrepancies in the various reports were observed, but review of the descriptions of cultural characteristics shows that the organism noted as essential to the disease has varied from a fairly active fermenter to an absolute non-fermenter, and that the action on milk and the pathogenicity have also been variously described. At present the organism most often described as the rhinoscleroma bacillus does not form gas in sugar media, does not coagulate milk, and is of variable, but in general feeble, pathogenicity.

The case which afforded material for this paper came to Dr. W. H. Marvin, of Cleveland, in the spring of 1905. The patient was a Slav from eastern Austria, 35 years of age, and had suffered from the disease before his arrival in America two years previously. The growths, which were in every way typical, had caused so much narrowing of the larynx that tracheotomy was necessary. At the time of the operation Dr. W. T. Howard, Jr., was asked to be present, and it is to his courtesy and to that of Dr. Marvin that I am indebted for my material.

At the time of the operation cultures were made from the surface of the growths in the nose, and immediately afterward from deeper parts after suitable aseptic precautions. A large number of plates were made from these cultures, and the growths themselves were preserved for microscopic examination.

Coverslips from the inside of the nose, from the surface of the growths, and from the depths of the lesion showed varying numbers of short bacilli mostly in pairs, with well-marked capsules, a few cocci, and a few slender uncapsulated bacilli. All except the cocci decolorized by Gram. The plates from the different sources gave practically indistinguishable growths, except that those from the depths of the lesion were almost free from cocci; the characteristic colony was large, flat, transparent, sharply defined, with a moist appearance, and on coverslip showed capsulated diplo-bacilli. The cocci noted in the coverslips were identified as the ordinary pyogenic forms, and the non-capsulated bacilli were found to be actively motile, and were later identified as colon bacilli.

Of the non-motile, capsulated forms, 12 cultures were selected on account of slight differences in the appearance of the colonies. These were denoted by letters, as were also such organisms as were studied for comparison later. These 12 were inoculated into the usual media and into fermentation tubes, with the result that they fell at once into three groups, one, including *C*, *E*, *F*, *G*, *K*, *M*, *N*, and *X* answered to my *Bact. aërogenes* group, fermenting dextrose, lactose, and saccharose with gas formation, a second group *A* and *B*, fermenting dextrose only, and a third, *D* and *Z*, apparently unable to form gas in any of the sugars. As a result of this preliminary work, *E* and *X* were taken as representatives of Group 1, *A* of Group 2, and *D* and *Z* of Group 3.

During the course of the work several organisms of the group were obtained from various sources and cultivated by way of comparison. Of these strains, *O* and *S* were grown from cases of turbinate hypertrophy, in no way related to rhinoscleroma, and *R* was found in a guinea-pig confined with other pigs inoculated with members of the series. As a further comparison, cultures of Edward's *Bacterium mucogenum* were obtained, one in 1905, one in 1906, through the courtesy of Dr. W. W. Ford of Johns Hopkins.

The present paper treats of the cultural reactions and the differentiation of these organisms from one another and from organisms of the same group obtained from other sources, of the relation of the bacteria in the tissue to the lesions, and presents a general discussion of the group. These points will be dealt with separately.

Bacteriological technique.—The routine laboratory media, used fresh and slightly alkaline to litmus were found to give very favorable growths. In the fermentation tests, however, dextrose-free broths were used as a basis, with dextrose, lactose, and saccharose in the proportion of 1 per cent for differentiation. The dextrose was the usual powdered glucose, but the lactose and saccharose were tested to measure their freedom from dextrose. Merck's and Kahlbaum's were found satisfactory.

The broth was titrated to show a faint rose pink with phenolphthalein, and after fractional sterilization the reaction was found to be from +0.5 to +0.10, and the medium gave very active gas formation with fermenters from other groups. Each batch of media was tested with the stock culture of *B. aërogenes* as a control, and unless gas appeared in 24 hours, the batch was rejected.

It was found that sealing or capping the mouths of the tubes stimulated contamination by mold, so that it appeared to be more satisfactory to refill the bulbs from time to time with sterile distilled water. Whenever a series was refilled, 5 c.c. samples of the water were placed on agar, in broth, and in dextrose fermentation tubes and in no case was there any growth, thus proving the sterility of the water, a point the great importance of which will appear later.

The usual stains were tried, and the capsules were easily demonstrated by any of the current methods.

Histological.—The tissue was hardened in Zenker's and alcohol, cut in paraffin, and stained with hematoxylin eosin, eosin and methylene blue, Giemsa's stain, and Weigert's.

General characteristics.—Cultures were made on plain, glycerin, and dextrose agar, in gelatin, broth, and litmus milk, and on potato. The most conspicuous thing about the *agar cultures* with the exception of *A* and *B*, was the transparency of the growth, which has been noted by practically all observers in cultures from this disease. The streak, after 24 to 48 hours was broad, raised, almost the color of the agar, and in certain lights could hardly be seen. This was no more marked in *D* and *Z*, the non-fermenting varieties, than in the forms such as *X*, which fermented all three sugars. Growth in the stab was uniformly good, and in the dextrose fermenters gas was seen in the dextrose agar. The water of condensation was thickened, and usually viscid, though this viscidity varied with different strains and even in different sets of media, being most marked in *E* and least in *X*. The cultures *A* and *B* were more of the ordinary type, far whiter and more porcelain-like, with practically no viscidity. The growth on the slant in the more active strains had a tendency to show infolding at the edges, which, on account of the differences of refraction, gave the appearance of a mixed culture, but plating showed no contaminations. As the cultures grew older, the edges faded more and more, until they became almost indistinguishable, with a rather whiter line in the center, and a white sediment in the water of condensation. With the exception of the distinction between *A* and *B* and the rest, the agar cultures were insufficient to distinguish the varieties.

GELATIN stabs showed no liquefaction after six weeks. Some of the varieties showed more nail growth than others, notably *A* and *B*, but this depended more on the concentration of the gelatin than on any other detail.

BROTH gave uniform cloudiness, more marked on shaking, with a heavy, often viscid precipitate, and frequently with a slight pellicle or a more or less marked white ring at the surface. Indol was slight in this series but present in all.

POTATO in general showed rather poor growth unless the medium was made distinctly alkaline with a calculated quantity of NaOH, when the growth was profuse, spreading, moist, and, in the case of the more active gas formers, showed occasional gas bubbles. After a week or 10 days the potato usually became discolored.

MILK. Change of reaction was slow in this medium. The organisms fermenting lactose gave acid reaction after a variable number of days (see Table 3), but never to a degree sufficient for coagulation. The non-lactose fermenters acted variously.

A gave sharp alkali from the second day, increasing in intensity but never reaching a grade sufficient for solution of the casein, while *D* and *X* gave very slight acid at first, followed by a return to neutrality, after which there was no further change.

In general the cultural results on routine media were sufficient to distinguish *A* and *B* from the others, but not for any further differentiation. This agrees essentially and in detail with the results in my preceding paper, and leaves in the way of ordinary cultures, nothing but the fermentation test. The results in this line will be taken up more in detail.

GLYCERIN MEDIA, while very favorable to the growth of the organisms, showed gas only with the most active strains, indicating weakness in activity toward glycerin, borne out later by the fermentation tubes.

Pathogenicity.—Inoculations into animals were made from time to time, but with no idea of classification by that means, as previous experiments with this group showed the variability of the pathogenicity to be so great as to make this unsatisfactory. Several members of the different groups were inoculated in varying amounts into guinea-pigs and mice, in an attempt to reactivate the feeble ones, and the results are best summarized as follows:

A was found pathogenic for guinea-pigs, in intraperitoneal inoculations of 1 c.c. in 48 hours, and the recovered organisms acted culturally exactly like the original.

D showed variable activity, in one case killing a guinea-pig with 1 c.c. in less than 24 hours, and another failing to kill with a dose of 10 c.c. The recovered organisms showed no change.

G was resisted in a 5 c.c. dose at one trial and was fatal to a guinea-pig in a 1 c.c. dose in another case. No change in organism.

M killed guinea-pigs in 48 hours, with no change in the organism recovered.

X apparently the most virulent, killed in 1 c.c. doses in a few hours.

Z was resisted by guinea-pigs in small doses, but proved fatal in large ones.

During this series a new organism was obtained from a guinea-pig which had been inoculated with tuberculous lymph glands, and owing to a lack of room was in the same cage with pigs inoculated with *D* and *Z* respectively. The organism recovered was culturally similar to *Z*, the animals had bitten each other, and it was supposed that transmission of infection took place that way. This organism was, however, given the name of *R*, and found readily pathogenic for guinea-pigs in small amounts.

The autopsies on all these animals showed very similar lesions. There was congestion and cloudy swelling of the organs, with peritonitis of a greater or less degree, usually somewhat viscid, and showing capsulated organisms of the original type. The lymph glands were enlarged, and in *M* and *D*, acute pleurisy, with presence of the organisms in the exudate, was found, while in *X* the lesion was of the acute hemorrhagic type, this variety being by far the most virulent of the lot. In all these the organisms recovered showed no changes in their cultural reactions.

Edwards' 05 (inactive and active), were pathogenic to mice in small amounts, and the organisms showed no special changes, except that Edwards' 05 (inactive), was more profuse and moist, approaching more closely the activated form.

Analysis of these results shows that practically all the organisms isolated from the case were more or less pathogenic for animals, without regard to their fermentative action, and further that different members of the same fermentative group reacted differently toward animals, so that classification on this basis would give peculiar results. As far as could be seen, there was no increase of fermentation after passage through the animals, except possibly in the case of *R*, contrary to the findings in the former paper. It must be noted, however, that the cultures in this case were all direct from living tissues, while those noted before were old and decadent laboratory cultures.

It is important also to note that in no case was there any tendency to productive lesions, but the death of the animal occurred usually in two to five days, and the method of inoculation does not encourage the formation of that type of infection.

Fermentation tests.—The details of the different tests on dextrose, lactose, and saccharose may be found in the appended tables, but the results can be more clearly seen from a general discussion. It will be noted that in the table, *A* is used as representative of the group *A B*, because the two acted in an identical manner, but that although *X* was taken as representative of the group fermenting all three sugars, *E*, *G*, and *M*, of the same group, show differences which are worthy of note. In the same way *D* and *Z* are both recorded.

A was found to ferment dextrose quite readily, forming bubbles in dextrose agar in four to six days, and gas in the closed arm of the fermentation tube in 48 hours, while up to the end of 32 days there was no sign even of a cloud in the closed arm. These tests were made in the spring of 1905, and the stock culture of the organism died out in the summer so that no further tests could be made. I am therefore unwilling to state definitely that no fermentation would have occurred in further trials. The milk cultures were alkaline from the start, and there was marked alkalinity in the bulbs of the fermentation tubes, so it is at least probable that lactose was not fermented.

X, representative of the *Bact. aërogenes* group, fermented all three sugars with gas formation, but with markedly different reactions toward the different sugars, which variations were consistent. Dextrose was fermented in from 24 to 72 hours, while lactose required five to eight days, and saccharose eight to 22 days, in one case no fermentation of saccharose beyond the formation of a cloud being noted.

E, another representative of the same group, fermented dextrose in 48 hours to five days, lactose in 2 to 12 days, and saccharose in one case not at all, in other cases in 10 to 19 days. In neither of these strains was there any notable change during the different series, but in two other strains, *G* and *M*, there was an apparent loss of power, *G* fermenting dextrose readily in 48 hours throughout, but showing progressive slowness in saccharose from 2 to 11 days and then 20 days, while the lactose swung back and forth from eight to two to seven days. *M*, last in all the sugars, dextrose going from two to four days, lactose from two to five to seven days, and saccharose from 3 to 10 days, finally no fermentation taking place in 32 days.

D and *Z* consistently failed to form gas, though a cloud of singular persistence was seen in the closed arms of both the dextrose and saccharose tubes. At the end of 42 days the cultures were still alive, but no further change seemed to take place, the cloud remaining permanently.

Before going on to the results in the other group, it may be well to note certain details concerning two other organisms isolated from the nose in two cases of turbinate hypertrophy, the one, *S*, from the surface, the other, *O*, both from the surface and the depth of the mass. The cases were both chronic hypertrophic rhinitis of the usual type, the tissues in no way resembling those of rhinoscleroma. *S* was of the *Bact. aërogenes* type, as seen in the table, and fermented all three sugars readily in

24 hours, much as did the stock *Bact. aërogenes*. On the other hand, *O*, while it made gas readily in dextrose and glycerin agar, took 6 to 12 days to form gas in dextrose fermentation tubes, gave no change in 25 days in lactose or saccharose, made milk sharply alkaline, and failed to make gas aerobically in 1 per cent saccharose agar. In growth and in morphology it closely resembled *A*. This organism was obtained late in the year, and repetition of the fermentation was not possible on account of lack of time, but it appears to be a dextrose fermenter only.

Here then we have a series of organisms fermenting in varying degrees, and each one varying according to the suitability of the medium. *D* and *Z* form a cloud in dextrose and saccharose, indicating some degree of fermentation, but not to the point of gas formation. *A* and *O* form gas in dextrose, but are apparently unable to break up the double sugars. In the others we have a progressive series of activity from *M* through *G* to *E* and then *X*, culminating in the very active *S*.

With this suggestive basis we come to the next series of fermentations. These deal with organisms of the mucosus capsulatus group supposed by others, or by myself, to be completely inactive toward all three sugars, more so even than *D* or *Z*. This set includes *R*, Edwards' 05 and Edwards' 06. As seen in the table, in the first two trials *R* showed not even a cloud in the stem, and similar claim is made by Edwards for his organism, *Bact. mucogenum*. The first two were inoculated routinely into fermentation tubes made up from dextrose-free broth which had stood in a sealed flask from May until January. The tubes were inoculated in the usual way and for nine days no change was noted. At that time, owing to evaporation, the bulbs were found to be nearly empty and were filled with distilled water, control inoculation being made as described under *Technique*. The next day a cloud was seen in the dextrose of Edwards' 05 and two days later in that of *R*. The next day gas appeared in *R*, increasing for two more days, up to which time the only change in Edwards' 05 was increased density of the cloud. Thirteen days after the filling-up with water, gas began to appear in Edwards' 05 dextrose, *21 days from inoculation*, and on this day there appeared in the saccharose of *R*, with a cloud in the lactose. This cloud increased the next day, with the formation of gas and the simultaneous appearance of gas in the lactose of Edwards' 05. The saccharose tube of the latter showed a marked cloud. *Forty-two* days after inoculation the saccharose of Edwards' 05 still showed no gas, but became infected with mold and had to be discarded.

These surprising activities were looked on with great suspicion as probable contaminations, and steps were taken to find out if such were present. Plates made from the dextrose of Edwards' 05 and of *R*, from the saccharose of Edwards' 05 and the lactose of *R*, showed in the first three cases contamination to a moderate degree with a spore-bearing bacillus, having a tendency to thread forms. The only other organism present besides the spore bearer in each tube was a short diplo-bacillus similar to the original. In the lactose of *R* only the diplo-bacillus was found. Isolation of the different species showed that the contaminations were not identical, practically excluding a common source. The diplo-bacilli grew out in large, round, moist colonies in which they were distinctly capsulated, and all the colonies were alike except those from the saccharose of Edwards' 05. Inoculations were made into dextrose fermentation tubes and into dextrose and glycerin agar, and it was found that the diplo-bacilli fermented with more rapid gas formation than any of the others previously noted, while the contaminating spore-bearers formed no gas in three weeks and were apparently purely aerobic in their growth. The diplo-bacilli from the saccharose of Edwards' 05 did not form gas, but showed a more profuse and moist growth than previously.

At a later time the evaporating tubes of saccharose of *E* and *X*, which had not shown any gas formation, were refilled with sterile water, and a few days later gas began to appear. Plates from these showed pure cultures of the original organisms.

This series of results is the chief interest of the paper. To resume it in brief, we have first a series of fermentation-tubes nine or more days old, which have shown no sign of gas formation. On account of evaporation of the fluid in the bulb, the portion lost was replaced with water, proved sterile, and in a period varying from two to 14 days signs of activity appeared. Careful plating showed most of the tubes to be completely uncontaminated, and furthermore showed that such contaminations as were present were completely inactive as regards fermentation. The members of the *B M C* group found in the plates made from *E* and *X*, known as fermenters, showed no alteration from the originals when studied on the usual media, while those from *R* and from Edwards' 05 showed marked increase in activity, and an appearance on culture closely resembling the other members of the group.

Exclusion of the spore-bearing contaminations as agents in this active fermentation leaves us two alternatives, the first that the organism in question has become activated or reactivated, the other that there has been a contamination by a bacillus of the same group identical morphologically, but with fermentation and cultural characteristics not only unlike the organism originally inoculated in the tube, but even unlike any in stock before or since. Of the two possibilities, the former seems the more simple, but for further check another culture of Edwards' organism was requested from Baltimore, and on its arrival called Edwards' 06. Inoculation after several subcultures on glycerin agar resulted in gas formation in dextrose in 12 days, lactose in 14 days, and a cloud in saccharose, very similar to what occurred in the Edwards' 05. As a further check, Edwards' 05 was retested, and though after four weeks there was a cloud in the tubes, no gas was found, but after eight weeks (56 days) gas was formed and plates showed pure cultures, checked by coverslips and cultures on various media.

We then have *three separate cases* of reactivation, and, so far as I can see, all possibility of contamination has been removed. The discussion of the conclusions will be postponed to a later part of this article.

The cultural reactions of these reactivated organisms showed close similarity to the type of the rest of the group, and the growths in media containing sugar were of course modified. Acid was formed in milk in a few days, and gas appeared in glucose agar. A possible explanation for the absence of coagulation in milk, in spite of the active fermentation of lactose is that the alkali formation was still sufficiently active to keep the acid below the clotting percentage.

All the organisms of this series showed inability to ferment glycerin in 1 per cent solution in fermentation tubes, although the stock *Bact. aërogenes* gave one-fourth gas in 24 hours, with subsequent increase. In the former paper it was noted that the old laboratory cultures reactivated by passage through animals showed their greatest loss of power in their action on glycerin.

Acid formation.—Bertarelli,[1] in a recent paper, has classified the organisms of this group according to their acid formation, and a series including *S*, Edwards' 05 (activated), *O R* (activated) with *Bact. aërogenes* and *Bact. acidi lactici* as checks was run through fermentation-tubes from two sources of meat, and Edwards' 06, *R*, Edwards'

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[1] *Centralbl. f. Bakt.*, 1905–6, 37, p. 338.

05 (activated), and *O* from another source of meat. Where gas was formed, the titration with N/10 NaOH and phenolphthalein was done as soon as the maximum gas formation was reached, before the alkali growth in the bulb could change the closed arm reaction. When there was no gas formation, the reaction was tested at the end of two weeks. No elaborate analysis of the series will be made, as the variations with the different meats were well marked, and by judicious selection the organism could be arranged in almost any classification one chose, except, of course, that the non-fermenters *D* and *Z*, and the inactive *R* and Edwards' 05, fell into a class by themselves on account of the absence of acid.

The fluids from the bulb and closed arm were titrated separately, the latter being drawn off through a curved pipette without allowing it to flow into the bulb. The greatest amount of N/10 NaOH required to neutralize 5 c.c. was 2.5 c.c. and most of the reactions fell between 0.8 c.c. and 2.0 c.c.

In Bertarelli's paper the limits given were wide enough for each group to allow of plenty of doubtful cases at the borders. In general the acid formation is roughly in proportion to the relative amount of H in the formula H/CO_2.

Pathological histology.—Hardened sections from Dr. Marvin's case showed an intact, but somewhat swollen, mucous membrane, beneath which lay new-formed granulation tissue, with a good deal of fully developed connective tissue. The usual text-book description of rhinoscleroma applied to the structure of the mass. In sections stained with eosin and methylene blue, with Giemsa, and to a less extent with hematoxylin and eosin, numerous short, round-ended bacilli were seen, singly and in pairs, both in the "Mikulicz cells" and in lymph spaces. These bacilli were apparently for the most part capsulated. Gram's stain in *alcohol*-hardened tissues showed no organisms, while in the sections hardened in Zenker's, the organisms were visible but not unduly conspicuous.

The stress laid on the presence of the bacteria in the lesions as an indication of the etiological relations to the disease led to the study of sections of other nasal hypertrophies, not rhinoscleroma.

In one case of ordinary *nasal polyp*, somewhat inflamed, eosin-methylene blue showed bacilli and streptococci in the depths of the lesion under a nearly intact mucosa. Four other non-inflamed polypi showed no organisms. In two cases of marked *turbinate hypertrophy*, obtained through the courtesy of Dr. J. M. Ingersoll and Dr. W. T. Chamberlin, organisms of the *B M C* group were obtained, in one case from the surface, in the other from both surface and depths, and in the latter case capsulated diplo-bacilli were found throughout the tissue in sections. The organism in the latter case is that referred to as *O*. In the other case, denoted as *S*, no organisms were found in the sections.

DISCUSSION OF RESULTS.

The conclusions drawn from study of the literature and personal work fall under two heads, the relation of organisms of the *B M C* type to rhinoscleroma, and the relation of apparently non-fermenting organisms of this group to the fermenting varieties.

1. In rhinoscleroma we have a disease with lesions of the infectious

granuloma type, covered with intact mucous membrane, and containing, in special cells and in spaces, bacilli in pairs, with capsules. These bacilli show a variable reaction to Gram according to the hardening method. Cultures from the inside of the tumor-like masses have given growths of diplo-bacilli which had the essential characteristics of the *B M C* group, and were further similar in their pale transparent growth on slant agar. Important differences have, however, been noted by different authors in the fermentation activities. Some of the cultures have been pathogenic, others not so. Transmission of the disease in human beings by means of cultures of the organism has been uniformly unsuccessful, and only one or two successful animal experiments have been reported, none of which appear conclusive.

The endemic quality of the disease, the apparent absence of transmission by contact, in spite of the numbers of organisms in the nasal exudate, and the sporadic type of the disease outside its narrow endemic limits are all against the rhinoscleroma bacillus as a causative factor.

Furthermore, the organisms of this group are well known in disease, but in no case that I have been able to find have there been any lesions of a *productive* type, the only granulation tissue being that which fills up defects after a loss of tissue. General bacteremias, even hemorrhagic in type, are described, but aside from these the typical infection with *B M C* is a pyogenic one, whether in open or closed cavities. This holds good throughout, in the genito-urinary system, the gastro-intestinal tract and peritoneum, and also in the upper and lower respiratory passages, as noted by many authors, in antrum disease, pneumonia, and so forth. In these affections there is always more or less loss of mucosa. Accordingly, if rhinoscleroma *is* caused by an organism of this group, it is in every way a marked exception to other lesions due to the mucosus capsulatus series.

From the pure bacteriological standpoint, authors are not in agreement as to essential details of identification, and even in the present single case several varieties have been found. It seems more easily conceivable that several varieties of organisms living saprophytically in the nasal cavity should have been taken into the tissues mechanically, than that the lesion is due to the joint effects of several members of one group, especially when the disease has as definite an entity as has rhinoscleroma.

Numerous observers have noted organisms of the rhinoscleroma type in lesions bearing no relation to the disease, and in normal cases. In this paper, *O*, which closely resembles *A*, came from ordinary turbinate hypertrophy, and *S*, resembling *Bact. aërogenes*, from another similar case.

This leaves, so far as I can see, all of Koch's laws unfulfilled, as while organisms of the same general type are found in all cases, they are multiple or non-identical, they do not reproduce the disease when inoculated, and accordingly cannot be obtained from experimental lesions. The weight of the argument based on the finding of the organism in the depths of the tissues seems to me to be seriously affected by my finding organisms in the hardened tissues in a case of turbinate hypertrophy, and an inflamed nasal polyp.

In fine, the evidence obtained from my own work and that of others leads me to believe that the rhinoscleroma bacillus and the disease of rhinoscleroma have no etiological relation, the presence of the bacteria in the cells being due to secondary invasion or ingestion rather than to infection.

2. On the basis of my classification in the former paper, the *B M C* group was divided into three divisions, *Bact. aërogenes*, forming gas in all sugars, *Bact. pneumonicum*, forming gas in dextrose and saccharose, and *Bact. acidi lactici*,* forming gas in dextrose and lactose. The suggestion was made that *Bact. aërogenes*, rather than *Bact. pneumonicum* was the prototype of the group, the others having lost through adaptation, the power to ferment one or the other sugar. It was also stated to be the opinion of the author that the non-fermenting varieties of this group were degenerated or modified fermenters, rather than distinct entities. This was based

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* The organism spoken of in this and the preceding papers under the name of *Bact. acidi lactici* differs from the original *Bact. acidi lactici* of Hueppe, in that it forms no spores, but all the cultures I have been able to obtain under this name, whether from Kràl or elsewhere have been alike in this characteristic.

If spores could be demonstrated in the cultures, this finding would at once put the organism out of the *BMC* group, and the name for the third division would have to be changed.

partly on analogy, and partly on the revivification of some old laboratory cultures from Kràl, and the absence of any fermentation in certain cultures obtained from Baltimore with a history of fermentation.

Since the appearance of this paper, Edwards[1] has noted in three cases organisms of this group as etiological factors in acute infections. These organisms, while of the *B M C* group in all other ways, did not ferment, a fact upon which Edwards based the theory that there was a distinct variety of *B M C* which was pathogenic and non-fermenting, and which, on account of its pathogenicity, deserved a position of its own. This organism was given the name of *Bact. mucogenum*, Edwards.

No statement is made as to the source of the media used by Edwards, or the length of time of the fermentation, but it is apparent from the present article that this makes a great difference, as my organisms were extremely weak fermenters in the ordinary Liebig extract broth, and even under most favorable circumstances showed extremely delayed reactions. Two cultures of Edwards obtained a year apart, from Baltimore, were found to ferment after several weeks in favorable meat extracted broth, while in ordinary broth no fermentation took place. This was also true with an organism in my own series. In fact, taking my own series and Edwards organism together, we have organisms which form:

1. Cloud but no gas in *D* and *S*, no cloud in *L*.
2. Gas in *D*, aerobically or in closed arm, no cloud in *L* or *S*.
3. Gas in *D* readily aerobically, very closely in closed arm, no cloud in *L* or *S*.
4. Gas in *D*, *L*, and *S*, with long-delayed reaction, especially noteworthy in *S*.
5. Gas after several weeks in *D*, *L*, and *S*, after which they fall into a class between 4 and 6 in activity.
6. Gas readily in all three sugars.

It thus appears that one may find all grades of activity, and that activity may be restored to an organism which has lost it, either by passage through animals, or by long-continued culture in special media, though not in all cases; furthermore that many organisms, of this group at least, may be set aside as non-fermenters, either from the use of unsuitable media, or insufficient duration of growth.

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[1] *Jour. Infect. Dis.*, 1905, 2, p. 431.

In this connection it is of interest to note that organisms which lack power of gas-formation in lactose only, or saccharose only, have in my experience retained their characteristics unchanged, the organisms described in the former paper under those heads being unchanged after three years. All the organisms reactivated in the present series took on a modified aërogenes type.

All this brings up the complicated subject of classification. I notice that in a recent work on milk, it is often stated that the *Bact. acidi lactici* is a variety of *Bact. aërogenes*, and on that basis there is no reason for placing the Friedländer organism, which differs only in the sugar unaffected, in a class by itself.

TABLE I.

PERIOD IN DAYS BETWEEN INOCULATION AND GAS FORMATION.

NAME	1905 March 8	Apr. 16	May 10	May 11	1906 Jan. 22	Feb. 9	Feb. 28	Apr. 10	Apr. 24
A..........	D+2		(Dextrose agar) 6	+ 4					
	L o			o 32					
	S o			o					
D..........	D	o 23	o	o 32	o 42		o 17		
	L	o		o	o		o		
	S	o		o	o	o 21	o		
E..........	D+2	+	+	+ 5	+ 2	+ 3			
	L+2	+ 5		+ 5 12	+ 7				
	S o	+ 13		+ 16	+ 19	+10			
G..........	D+2	+ 2	+	+					
	L+8	+ 2		+ 7					
	S+2	+ 11		+ 20					
M..........	D+2	+	+	+ 4					
	L+2	+ 2		+ 5 7					
	S+3	+ 10		o 32					
X..........	D	+	+	+ 2	+ 1	+ 3			
	L	+ 8		+ 6	+ 5				
	S	+ 8		o + 22 +	+ 19	+17			
Z..........	D	o 25	o	o 32	o 42		o 17		
	L	o		o	o	o 27	o		
	S	o		o	o		o		
R..........	D	o 20	o	o 32	+ 13	+ 3	+ 2	+ 3	+ 2
	L	o		o	+ 22		+ 3	+ 6	+ 6
	S	o		o	+ 19		+ 3	+ 3	+ 2
Edwards' 05..	D				+ 21	+ 2	+ 2	+ 3	+ 1
	L				+ 22		+ 7	+ 4	+ 6
	S				o 42		+ 3	+ 4	+ 6
S..........	D						+ 1		+ 1
	L						+ 1		+ 1
	S						+ 1		+ 1
O..........	D							+11	+ 6
	L							o	o 10
	S							o	o
Edwards' 06..	D							+12	
	L							+14	
	S							o 23	
Edwards' 05..	(repeat)								
	D							+12	
	L							+14	
	S							o 14	

TABLE 2.

FERMENTATIONS.

Name	Sugar	Cloud Appeared in	Gas Appeared in (Average)	Total Gas	H/CO_2	Reaction of Stem
A	D	1 day	2-4 days	0.50	1/1	+
	L	No	No gas	....	...	−
	S	"	" "	....	...	−
D	D	1 day	None in 42 days	....	...	±
	L	No	" " 42 "	....	...	±
	S	7 days	" " 42 "	....	...	±
E	D	1-2 day	3 days	0.34	2/1	+
	L	3 days	6 "	0.33	3/1	+
	S	10 "	15 "	0.33	2/1	+
G	D	1 day	2 "	0.33	2/1	+
	L	2 days	6 "	0.25	5/3	+
	S	10 "	11 "	0.45	3/1	+
M	D	2 "	3 "	0.25	2/1	+
	L	3 "	5 "	0.33	2/1	+
	S	8+"	10+"	0.25	2/1	+
O	D	5 "	8 "	0.50	2/1	+
	L	No	No gas	0.00	...	±
	S	Slight 8 days	" "	0.00	...	±
R inactive	D	12 days	13+days	0.33	2/1	+
	L	19 "	20 "	0.33	3/1	+
	S	17 "	21 "	0.20	4/1	+
R active	D	1 day	2-3 "	0.50	2/1	+
	L	2 days	2-5 "	0.50	2/1	+
	S	2 "	3 "	0.60	3/1	+
S	D	1 day	1 day	0.45	3/1	+
	L	1 "	1 "	0.40	3/1	+
	S	1 "	1 "	0.40	2/1	+
X	D	1 "	2 days	0.27	2/1	+
	L	4 days	7 "	0.33	2/1	+
	S		17+"	0.40	3/2	+
Z	D	1 day	None in 42 days	0.00	...	±
	L	No	" " 42 "	0.00	...	±
	S	3-6 day	" " 42 "	0.00	...	±
Edwards' 05, inactive	D	9 days	21+days	?	?	+
	L	21 "	22+ "	0.33	2/1	+
	S	22 "	42+ "	0.00	...	±
Edwards' 05, active	D	1 day	2 "	0.40	2/1	+
	L	3 days	6 "	0.40	2/1	+
	S	2 "	5 "	0.50	3/1	+
Edwards' 06	D	11 "	12 "	0.60	?	+
	L	13 "	14 "	0.50	?	+
	S	11 "	None in 23 days	0.00	?	±
Bact. aërogenes (stock)	D	1 day	1 day	0.8	?	+
	L	1 "	1 "	0.6	?	+
	S	1 "	1 "	0.9	?	+

TABLE 3.

MILK REACTIONS.

Name	Acid Reaction in	Coagulation in	Alkaline Reaction in	Permanently Amphoteric
A	......	......	2-5 days	
B	......	......	2-5 "	
C	2 days			
D	......	......	......	4 weeks
E	1-2 days			
G	1-2 "			
M	1-2 "			
O	......	......	2 days	
R inactive	......	......	6-10 "	
R active	1-2 days			
S	1 day	1-2 days		
X	1-3 days			
Z	......	......	......	4 weeks
Edwards' 05 inactive	......	......	5-12 days	
Edwards' 05 active	1-2 days			
Edwards' 06	Slight 2 days			
Bact. aërogenes (stock)	1 day	1-2 days		

CONCLUSIONS.

1. The so-called rhinoscleroma bacillus has no etiological relation to the disease of rhinoscleroma, but is rather a secondary invader.

2. The organisms found in the nose and nasal growths in rhinoscleroma are different in different cases, though of the same general group.

3. Organisms with the power to break up sugars with gas formation may lose such power, in whole or in part, through modifications in environment.

4. Organisms of this group which show no fermentative power are probably degenerated rather than definite entities, and can in many cases be reactivated to their original type.

5. *Bact. aërogenes* is the prototype of the group, and by analogy with *B. coli communis* and *communior*, the other members may perhaps be considered as varieties of it.

6. Until *Bact. pneumonicum* or *Bact. acidi lactici* is activated into *Bact. aërogenes*, the classification formerly brought forward is apparently justified.